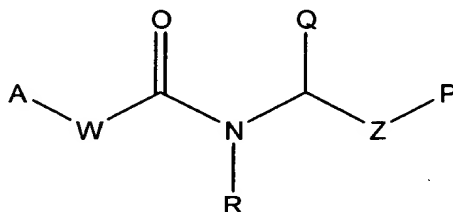


**AMENDMENTS TO THE CLAIMS**

1. (Currently Amended) A pharmaceutical composition comprising a compound of Formula I,



(I)

wherein

A is a MetAP-2 inhibitory core;

W is O or NR;

each R is, independently, hydrogen or alkyl;

Z is  $-\text{C}(\text{O})-$  or  $-\text{alkylene}-\text{C}(\text{O})-$ ;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is  $-\text{OR}$ , Q is not hydrogen;

or

Z is  $-\text{alkylene}-\text{O}-$  or  $-\text{alkylene}-\text{N}(\text{R})-$ ;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen;

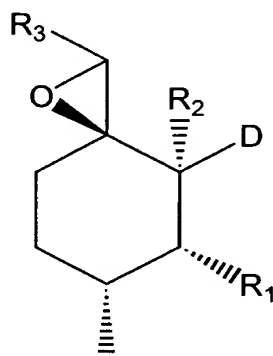
or a pharmaceutically acceptable salts thereof,

and a pharmaceutically acceptable carrier.

2. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1 wherein Z is  $-\text{C}(\text{O})-$  or  $\text{C}_1\text{-C}_4\text{-alkylene}-\text{C}(\text{O})-$ .

3. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 2 wherein Z is -C(O)- or C<sub>1</sub>-C<sub>2</sub>-alkylene-C(O)-.
4. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 2 wherein Q is linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl, phenyl or naphthyl.
5. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 4 wherein Q is isopropyl, phenyl or cyclohexyl.
6. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1 wherein Z is C<sub>1</sub>-C<sub>6</sub>-alkylene-O- or C<sub>1</sub>-C<sub>6</sub>-alkylene-NR-.
7. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 6 wherein Z is C<sub>1</sub>-C<sub>4</sub>-alkylene-O- or C<sub>1</sub>-C<sub>4</sub>-alkylene-NH-.
8. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 7 wherein Z is C<sub>1</sub>-C<sub>2</sub>-alkylene-O- or C<sub>1</sub>-C<sub>2</sub>-alkylene-NH.
9. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 6 wherein Q is linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl, phenyl or naphthyl.
10. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 9 wherein Q is isopropyl, phenyl or cyclohexyl.
11. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1 wherein each R is, independently, hydrogen or linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl.
12. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 11 wherein each R is, independently, hydrogen or linear or branched C<sub>1</sub>-C<sub>4</sub>-alkyl.
13. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 12 wherein each R is, independently, hydrogen or methyl.
14. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 13 wherein each R is hydrogen.

15. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1



wherein A is of Formula II,

(II)

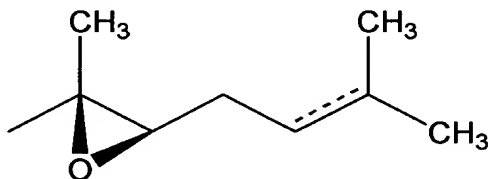
wherein

R<sub>1</sub> is hydrogen or alkoxy;

R<sub>2</sub> is hydrogen or hydroxy;

R<sub>3</sub> is hydrogen or alkyl; and

D is linear or branched alkyl or arylalkyl; or D is of the structure



16. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 15 wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>4</sub>-alkoxy.

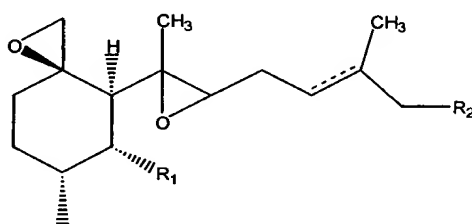
17. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 16 wherein R<sub>1</sub> is methoxy.

18. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 15 wherein R<sub>3</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl.

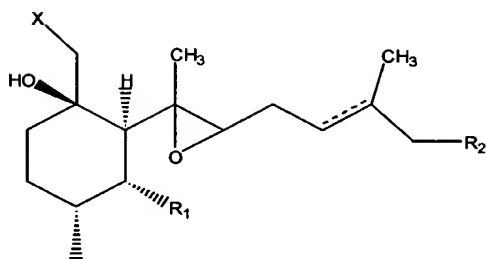
19. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 18 wherein R<sub>3</sub> is methyl.

20. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 15 wherein D is linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl; or aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl.

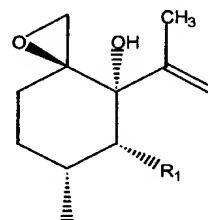
21. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1 wherein A is selected from the group consisting of



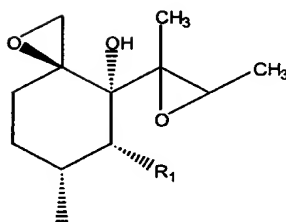
(IV)



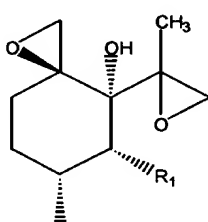
(V)



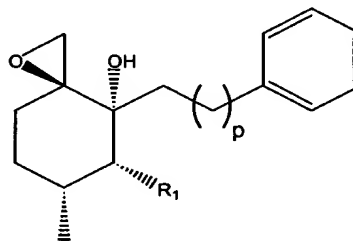
(VI)



(VII)



(VIII)



(IX)

wherein

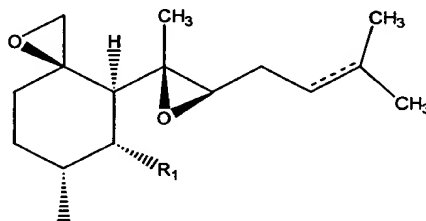
p is an integer from 0 to 10;

R<sub>1</sub> is hydrogen, -OH or C<sub>1</sub>-C<sub>4</sub>-alkoxy;

X is a leaving group; and

R<sub>2</sub> is H, OH, amino, C<sub>1</sub>-C<sub>4</sub>-alkylamino or di(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino).

22. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 21 wherein A is of the formula



23. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 1 wherein P comprises from 1 to about 20 amino acid residues.

24. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 23 wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

25. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 24 wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

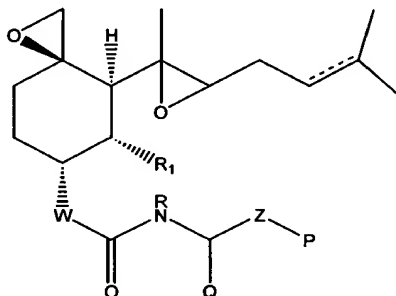
26. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 25 wherein the matrix metalloprotease is MMP-2 or MMP-9.

27. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 26 wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

28. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 27 wherein P comprises the a sequence selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5);

Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15); Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23).

29. (Currently Amended) A pharmaceutical composition comprising a compound of the formula



wherein

W is O or NR;

each R is, independently hydrogen or a C<sub>1</sub>-C<sub>4</sub>-alkyl;

Q is hydrogen; linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl; or aryl;

R<sub>1</sub> is hydroxy, C<sub>1</sub>-C<sub>4</sub>-alkoxy or halogen;

Z is -C(O)- or C<sub>1</sub>-C<sub>4</sub>-alkylene;

P is NHR, OR, or a peptide comprising 1 to 100 amino acid residues attached to Z at the N-terminus; or

Z is alkylene-O or alkylene-NR; and

P is hydrogen or peptide comprising 1 to 100 amino acid residues attached to Z at the C-terminus;

or a pharmaceutically acceptable salt thereof; provided that when P is hydrogen, NHR or OR, Q is not hydrogen;

and a pharmaceutically acceptable carrier.

30. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 29 wherein

W is O or NH;

Z is alkylene-O or alkylene-NH;

Q is isopropyl;

R<sub>1</sub> is methoxy; and

P comprises from 1 to 15 amino acid residues.

31. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 30 wherein

W is O; and

P comprises 10 or fewer amino acid residues.

32. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 29 wherein P comprises from 1 to about 20 amino acid residues.

33. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 32 wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

34. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 33 wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

35. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 34 wherein the matrix metalloprotease is MMP-2 or MMP-9.

36. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 35 wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

37. (Currently Amended) The ~~compound~~ pharmaceutical composition of Claim 36 wherein P comprises the a sequence selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-

Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15); Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23).

38. (Currently Amended) A pharmaceutical composition comprising a angiogenesis inhibitor-compound selected from the group consisting of

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxy-carbonylamino}-3-methyl-butyric acid methyl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxy-carbonylamino}-3-methyl-butyric acid methyl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxy-carbonylamino}-4-methyl-pentanoic acid methyl ester;

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxy-carbonylamino}-phenyl-acetic acid methyl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Hydroxymethyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl)oxycarbonylamino}-3,3-dimethyl-but-2-enoic acid methyl ester;

Cyclohexyl-2-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl)oxycarbonylamino}-acetic acid methyl ester;

2-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl)oxycarbonylamino}-3-methyl-pentanoic acid methyl ester;

[1-(1-Carbamoyl-2-hydroxy-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

2-(3-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl)-ureido)-3-methyl-but-2-enoic acid methyl ester;

2-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-((2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl)oxycarbonylamino}-3-methyl-but-2-enoic acid;

N-Carbamoyl (ID#31) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-((2*R*,3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#30) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-((2*R*,3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#32) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-((2*R*,3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#40) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-((2*R*,3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#39) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-((2*R*,3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl)-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#26) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#27) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#24)-(2*R*)-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#36)-(2*R*)-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

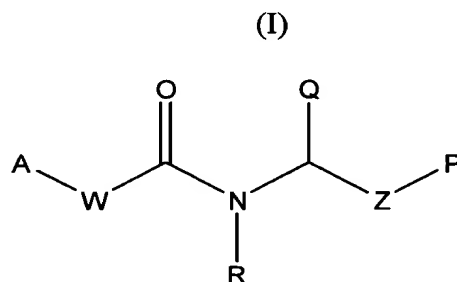
(ID#37)-(2*R*)-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#38)-(2*R*)-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester; and

(ID#34)-(2*R*)-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

and a pharmaceutically acceptable carrier.

39. (Currently Amended) A method of treating an angiogenic-disease in a subject, comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising the an-angiogenesis inhibitor compound comprising of Formula I and a pharmaceutically acceptable carrier.



wherein

A is a MetAP-2 inhibitory core;  
W is O or NR;  
each R is, independently, hydrogen or alkyl;  
Z is –C(O)- or -alkylene-C(O)-;  
P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;  
Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;  
or Z is –alkylene-O- or –alkylene-N(R)-;  
P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;  
Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen; and a pharmaceutically acceptable salt thereof,  
thereby treating the ~~angiogenic~~ disease in the subject.

40. (Original) The method of claim 39, wherein said angiogenic disease is an autoimmune disease.

41. (Original) The method of claim 40, wherein said autoimmune disease is rheumatoid arthritis.

42. (Original) The method of claim 39, wherein said angiogenic disease is cancer.

43. (Original) The method of claim 39, wherein said subject is a human.

44. (Canceled)

45. (Currently Amended) The method of claim 39, wherein the ~~angiogenesis inhibitor compound~~ pharmaceutical composition is administered to the subject intravenously.

46. (Currently Amended) The method of claim 39, wherein the ~~angiogenesis inhibitor compound~~ pharmaceutical composition is administered to the subject intramuscularly.

47. (Currently Amended) The method of claim 39, wherein the ~~angiogenesis inhibitor compound~~ pharmaceutical composition is administered to the subject orally.

48. (Currently Amended) The method of claim 39, wherein the ~~angiogenesis inhibitor~~ compound of Formula I is selected from the group consisting of

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino]-3-methyl-butyric acid methyl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino]-4-methyl-pentanoic acid methyl ester;

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-phenyl-acetic acid methyl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Hydroxymethyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino]-3,3-dimethyl-butyric acid methyl ester;

Cyclohexyl-2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino]-acetic acid methyl ester;

2-[(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino]-3-methyl-pentanoic acid methyl ester;

[1-(1-Carbamoyl-2-hydroxy-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-(3-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)-ureido)-3-methyl-butylamide;

2-((3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonylamino)-3-methyl-butyl acid;

N-Carbamoyl (ID#31) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#30) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#32) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#40) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#39) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#26) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

N-Carbamoyl (ID#27) (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#24)-(2*R*-((3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonyl) amino-3-methyl-butanol) ester;

(ID#36)-(2*R*-((3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonyl) amino-3-methyl-butanol) ester;

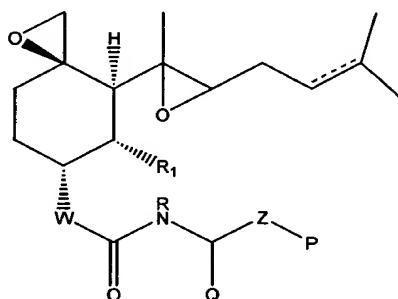
(ID#37)-(2*R*-((3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonyl) amino-3-methyl-butanol) ester;

(ID#38)-(2*R*-((3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonyl) amino-3-methyl-butanol) ester; and

(ID#34)-(2*R*-((3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2*R*,3*R*)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl)oxycarbonyl) amino-3-methyl-butanol) ester.

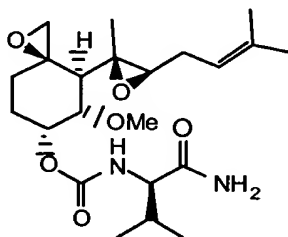
49. (New) The pharmaceutical composition of claim 29, wherein  
 W is O;  
 each R is, independently hydrogen;  
 Q is a linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl; or aryl;  
 R<sub>1</sub> is C<sub>1</sub>-alkoxy;  
 Z is -C(O);  
 P is NHR.

50. (New) A pharmaceutical composition comprising a compound of the structure



- and a pharmaceutically acceptable carrier, wherein  
 W is O;  
 each R is, independently hydrogen;  
 Q is a linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub>-alkyl; or aryl;  
 R<sub>1</sub> is C<sub>1</sub>-alkoxy;  
 Z is -C(O);  
 P is NHR;  
 or a pharmaceutically acceptable salt thereof.

51. (New) A pharmaceutical composition comprising a compound of the following



structure and a pharmaceutically acceptable carrier:

52. (New) A pharmaceutical composition comprising a compound of the structure (1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester, and a pharmaceutically acceptable carrier.

53. (New) The pharmaceutical composition of claim 1 formulated as a controlled release composition.

54. (New) The composition of claim 53 wherein said controlled release formulation is a microcapsule.

55. (New) The pharmaceutical composition of claim 52 formulated as a controlled release composition.

56. (New) The composition of claim 55 wherein said controlled release formulation is a microcapsule.

57. (New) The pharmaceutical composition of claim 1, further comprising a supplementary pharmaceutically active compound.

58. (New) The pharmaceutical composition of claim 57, wherein said supplementary pharmaceutically active compound is selected from the group consisting of Taxol, Paclitaxel, Actinomycin D, a antidiabetic agent, Tolbutamide, heparin, and a sulfated cyclodextrin.

59. (New) A method for treating an angiogenic disease in a subject comprising administering said subject a compound comprising the structure (1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester.

60. (New) The method of claim 59, wherein said compound is administered as a controlled release formulation.

61. (New) The method of Claim 39 wherein the compound of Formula I is of the structure

